RESPONSE

Applicant's representative apologizes for the inadvertent failure to respond to the species election with respect to the elected Group III claims. Applicant respectfully traverses the requirement for a species election with respect to pending claim 20. Applicant provisionally elects the species of "nucleic acid" (readable on claim 20).

There has been no showing and the Action provides no rationale for the listed ligands being patentably distinct. In particular, there appears to be no substantive difference between the putative species of nucleic acid, polynucleotide and oligonucleotide. Those species are chemically identical, the only distinction being one of length. Further, there is no bright-line distinction in the art between the lengths of nucleic acids, polynucleotides and oligonucleotides. A molecule of a given length may be characterized as either a nucleic acid or a polynucleotide, or alternatively as an oligonucleotide or a polynucleotide. For example, Principles of Biochemistry, 2nd Edition, pg. 329, Lehninger et al., 1993 (excerpt attached) states, "A short nucleic acid is referred to as an **oligonucleotide**. The definition of 'short' is somewhat arbitrary, but the term oligonucleotide is often used for polymers containing 50 or fewer nucleotides. A longer nucleic acid is called a **polynucleotide**." That standard text acknowledges that the distinction between oligonucleotides, polynucleotides and nucleic acids is "somewhat arbitrary" and uses the terms interchangeably.

Applicant requests that the species to be examined in the event no generic claim is found allowable at least include nucleic acid, polynucleotide and oligonucleotide.

The Office Action also required a species election with respect to the type of probes and the probe lengths recited in new claims 31-48. Applicant respectfully traverses. Applicant provisionally elects the species of "chemically modified oligonucleotide" (readable on claim 33)

with respect to the Group A species election requirement and the probe length of 6 nucleotides (readable on claims 35 and 39) for the Group B species election requirement

Under 35 U.S.C. §121, as discussed in MPEP §802.01, a species election may be required if two or more "independent and distinct" inventions are claimed in one application. "Independent" means that there is no disclosed relationship between the two or more subjects disclosed, that is, they are unconnected in design, operation or effect, for example: (1) species under a genus which species are not usable together as disclosed. "Distinct" means that two or more species are related, but are capable of separate manufacture, use or sale as claimed and are patentable over each other. For a species restriction requirement to be proper, the species must be patentably distinct from each other. [MPEP 806.04(h)]

The Office Action requires a species election to a single type of probe (i.e., those set forth in instant claim 33). Claim 33 lists probes comprised of oligonucleotides, chemically modified oligonucleotides, oligonucleotide analogs or peptide nucleic acids. The Action concludes that, "The species are distinct, each from the other, because their structures and modes of operation are different. For the different products (e.g. probe), they differ in their reactivity and the starting materials from which they are made."

Although the structures of, for example, oligonucleotides clearly differ from modified oligonucleotides, oligonucleotide analogs or peptide nucleic acids, Applicant traverses that the modes of operation are different. The mode of operation of the probes would be to hybridize to an analyte nucleic acid, polynucleotide or oligonucleotide and to be detected. The Action makes no showing and provides no rationale for asserting that hybridization to a nucleic acid would differ for an oligonucleotide versus a modified oligonucleotide, oligonucleotide analog or peptide nucleic acid. In each case, hybridization would occur through known base-pair hydrogen bonding,

determined by purine-pyrimidine interactions. The hydrogen bonding portions of the purine and pyrimidine moieties would not vary between the asserted species. As each type of probe could be labeled with an identical type of label, there is also no showing that detection of labeled probes would differ for oligonucleotides, oligonucleotide analogs, etc.

Applicant further submits that the species are usable together and therefore do not meet the definition of "independent". For example, a probe library could be comprised partially of oligonucleotides and partially of chemically modified oligonucleotides, so long as each different sequence could be distinguishably labeled.

Applicant submits that the putative species of probe type are neither independent nor distinct and requests reconsideration and withdrawal of the species election requirement. Refusal to withdraw the requirement constitutes a finding by the Office that each of the species is patentably distinct. For example, claims drawn to "oligonucleotide probes" would be patentable over claims drawn to "chemically modified oligonucleotide probes" and vice versa.

Applicant also traverses the species election requirement with respect to probe length. An oligonucleotide probe of, for example, 5 nucleotides in length would have the same fundamental chemical structure as an oligonucleotide probe of 6 nucleotides in length. Also, oligonucleotide probes of any length could be made from the same starting materials. While hybridization to a target would potentially occur at somewhat differing stringencies and temperatures, depending on probe length, the mode of operation of hydrogen bond interaction would be identical regardless of probe length. Further, a probe library could potentially comprise a mixture of probes of different lengths, so long as each different probe sequence was distinguishably labeled. Therefore, probes of different length are neither independent nor distinct and Applicant respectfully requests reconsideration and withdrawal of the species election requirement with respect to probe length.

Refusal to withdraw the species election would constitute a finding by the Office that probes of different length are patentably distinct, for example, that claims to probes of 6 nucleotides in length are patentable over claims to probes of 5 nucleotides in length.

Respectfully submitted,

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Principles of Biochemistry

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Cover: The active site of the proteolytic enzyme chymotrypsin, showing the substrate (blue and purple) and the amino acid residues (red and orange) critical to catalysis. Determination of the detailed reaction mechanism of this enzyme (described on pp. 223–226) helped to establish the general principles of enzyme action.

Frontispiece: A view of tobacco ribulose-1,5-bisphosphate carboxylase (rubisco). This enzyme is central to photosynthetic carbon dioxide fixation; it is the most abundant enzyme in the biosphere. Different subunits are shown in blues and grays. Important active site residues are shown in red. Sulfates bound at the active site (an artifact of the crystallization procedure) are shown in yellow.

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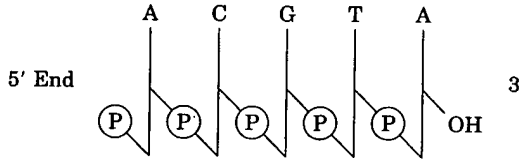
All the phosphodiester linkages in DNA and RNA strands have the same orientation along the chain (Fig. 12–7), giving each linear nucleic acid strand a specific polarity and distinct 5′ and 3′ ends. By definition, the **5′ end** lacks a nucleotide at the 5′ position, and the **3′ end** lacks a nucleotide at the 3′ position (Fig. 12–7). Other groups (most often one or more phosphates) may be present on one or both ends.

The covalent backbone of DNA and RNA is subject to slow, nonenzymatic hydrolysis of the phosphodiester bonds. In the test tube, RNA is hydrolyzed rapidly under alkaline conditions, but DNA is not; the 2′-hydroxyl groups in RNA (absent in DNA) are directly involved in the process. Cyclic 2′,3′-monophosphates are the first products of the action of alkali on RNA, and are rapidly hydrolyzed further to yield a mixture of 2′- and 3′-nucleoside monophosphates (Fig. 12–8).

The nucleotide sequences of nucleic acids can be represented schematically, as illustrated (at right) by a segment of DNA having five nucleotide units. The phosphate groups are symbolized by Ⓟ and each deoxyribose by a vertical line. The carbons in the deoxyribose are represented from 1′ at the top to 5′ at the bottom of the vertical line (even though the sugar is always in its closed-ring β-furanose form in nucleic acids). The connecting lines between nucleotides (through Ⓟ) are drawn diagonally from the middle (3′) of the deoxyribose of one nucleotide to the bottom (5′) of the next. By convention, the structure of a single strand of nucleic acid is always written with the 5′ end at the left and the 3′ end at the right; i.e., in the 5′→3′ direction. Some simpler representations of the pentadeoxyribonucleotide illustrated are pA-C-G-T-A_{OH}, pApCpGpTpA, and pACGTA. A short nucleic acid is referred to as an **oligonucleotide.** The definition of "short" is somewhat arbitrary, but the term oligonucleotide is often used for polymers containing 50 or fewer nucleotides. A longer nucleic acid is called a **polynucleotide.**



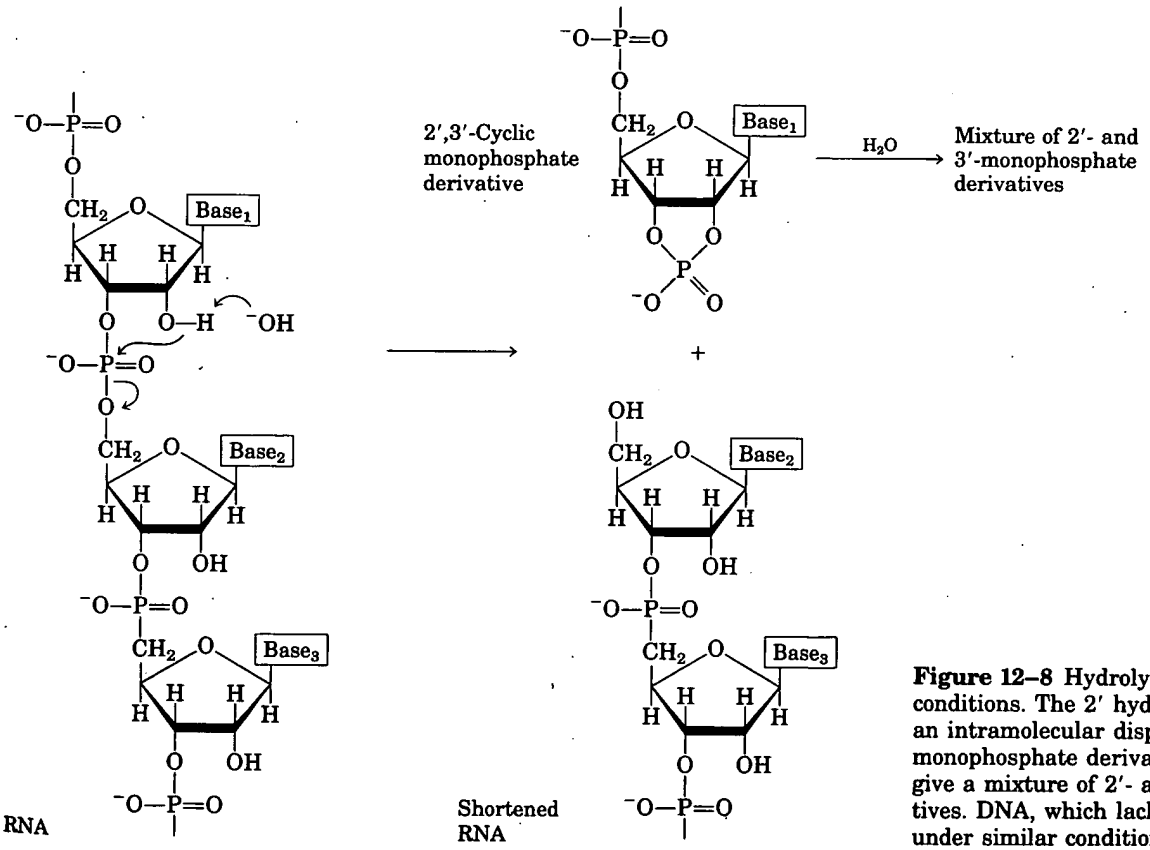


Figure 12–8 Hydrolysis of RNA under alkaline conditions. The 2′ hydroxyl acts as a nucleophile an intramolecular displacement, the 2′,3′-cyclic monophosphate derivative is further hydrolyzed t give a mixture of 2′- and 3′-monophosphate deriv tives. DNA, which lacks 2′ hydroxyls, is stable under similar conditions.